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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/444,790	03/19/95	BROCKHAUS	9189

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18N2/0203

EXAMINER

BASHAM, D

ART UNIT

PAPER NUMBER

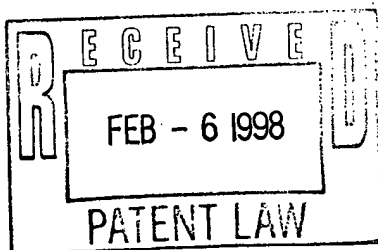
1812

DATE MAILED: 02/03/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

RESPONSE DUE: <u>May 3, 1998</u>
STATUTORY PERIOD EXPIRES: <u>August 3, 1998</u>



Copy Sent to
Department PLP

Applicant's app

Office Action Summary

Application No.
08/444,790

Applicant(s)
Brockhaus, et al.

Examiner
Daryl A. Basham

Group Art Unit
1812



☒ Responsive to communication(s) filed on Nov 7, 1997

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 44-47 and 55-59 is/are pending in the application.

Of the above, claim(s) 55 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 44-46 and 56-58 is/are rejected.

☒ Claim(s) 47 and 59 is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1812

DETAILED ACTION

1. Please note the Examiner and Art Unit handling this case has changed. Please direct all further communications to the below named Examiner. The amendment filed November 7, 1997 has been entered.

2. RESPONSE TO REMARKS

Applicant's arguments filed November 7, 1997 have been fully considered and are deemed not to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 44 and 46 are again rejected and new claim 58 is rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al (B). The rejection of record is maintained, and the following reasons address the amendments.

Applicants arguments suggest that the Smith, et al. reference does not disclose every element of the invention claimed, citing *In re Marshall*, 198 USPQ 334 (CCPA 1978) and *Ex parte Levy*, 17 USPQ2d 1462 (BPAI 1990). However, the present facts are distinguished from *In re Marshall* because, as there are no structural limitations in the claims, one of skill in the art would recognize that the human 55 kDa TNF-R as taught by Smith, et al., at column 1, lines 7-10, has the identical properties enumerated in the instant claims: i.e., the receptor is a

Art Unit: 1812

homogenous preparation of a TNF binding receptor (as cloning would anticipate isolation since a pure polypeptide could be obtained from the deduced amino acid sequence by synthetic means), is insoluble as defined by the instant disclosure (e.g., naturally occurring membrane component, at page 7, lines 13-18 of the instant specification) and has the molecular weight of about 55 kDa in non reducing SDS-PAGE, as said electrophoresis means was used to purify and sequence the recited receptor (see Loetscher, et al. Cell (1990) Vol 61: pp. 351-359). Moreover, as Loetscher, et al., provide the basis in fact to reasonably support the determination of the essential characteristics inherently possessed by the 55 kDa receptor recited by Smith, et al., this case is also distinguished from Ex Parte Levy. For these reasons the rejection of record is maintained.

Claim Rejections - 35 USC § 112

4. Claims 44, 45 and 56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for membrane fraction comprising TNF receptors or detergent solubilized functional TNF receptors of defined structure, does not reasonably provide enablement for insoluble homogenous TNF receptors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification explicitly discloses that the instant protein is extracted from cells in detergent and that such a fraction is then solubilized in TX-100 containing buffers (see Example 2 or at page 13, lines 1-6 wherein a range of detergent agents is disclosed). Moreover, it is the

Art Unit: 1812

solubilized material that is affinity purified (e.g., Example 4), not an insoluble form (e.g., naturally occurring, membrane bound; at page 7, lines 13-18, cannot be at the same time homogenous), and as the receptor remains in detergent throughout further purification steps (e.g., Example 5, i.e., octylglucoside), there is no disclosure in which a homogenous insoluble form of the receptor is obtained or used. Therefore, as the specification fails to provide guidance or examples of how to make an insoluble homogenous form of the instant receptor, one of ordinary skill in the art could not make such a composition without undue experimentation as one would not expect a naturally occurring membrane to comprise but a single protein (e.g., homogenous) nor would one expect that a receptor that is not membrane bound to function in the absence of solubilization by detergent or other agent.

5. Claims 44, 46, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the TNF receptor polypeptide identified by sequences set forth in **Figures 1 and 4** or comprising specific enumerated amino acid or encoded by delimited nucleic acid sequences, does not reasonably provide enablement for all of the polypeptides which are 55 kDa which bind to TNF. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants suggest that the claims recite limitations which would exclude the instant TNF receptor from other TNF binding proteins. However, the apparent molecular weight limitation does not effectively distinguish the instant receptor because in the absence of kinetic constants

Art Unit: 1812

(e.g., K_D), sequence/structural information, signaling capabilities, and/or other properties which are *peculiar* to the instant receptor, other undisclosed polypeptides are embraced by the claim. For example, a membrane bound antibody fragment which is detergent solubilized (or secreted antibody fragment), wherein said antibody fragment binds to TNF and has an apparent molecular weight of 55 kDa would be embraced by the claims, however, such a polypeptide is could not be envisaged by the instant disclosure. Therefore, as the specification fails to provide guidance or examples of polypeptides which are not receptors comprising the structural delimitations of or domains comprised in instant **Figures 1 and 4**, the skilled artisan could not make all of the polypeptides commensurate in scope with the claims as a TNF receptor could not be distinguished from unrelated polypeptides having shared apparent molecular weight or similar gross binding properties.

6. Claims 44, 45 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44, 45 and 56 are vague and ambiguous because it is not clear as to how a receptor preparation can at once be insoluble as defined in the specification (naturally occurring membrane component, at page 7, lines 13-18) and homogenous, since a natural membrane would comprise many different proteins.

Art Unit: 1812

7. Claims 47 and 59 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daryl A. Basham, Ph.D., whose telephone number is (703) 305-2150. The examiner can normally be reached Monday through Friday from 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957.


Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [stephen.walsh@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

dab
February 2, 1998


STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800